### Male Liver Top 10 GO Biological Process Gene Sets Ranked by Potency of Perturbation (Sorted by BMD Median)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Category Name** | Input Genes/Platform Genes in Gene Set | % Gene Set Coverage | Active Genes | BMD1std Median of Gene Set Transcripts (mg/kg) | Median BMDL1Std-BMDU1Std (mg/kg) | Genes with Changed Direction Up | Genes with Changed Direction Down |
| **GO:0030278**regulation of ossification | 3/58 | 5% | mgp; id2; cebpd | 5.660 | 2.158-16.350 | 1 | 2 |
| **GO:0001822**kidney development | 4/53 | 8% | zfp354a; id2; egr1; aldh1a1 | 5.765 | 1.618-28.410 | 2 | 2 |
| **GO:1903707**negative regulation of hemopoiesis | 3/48 | 6% | pf4; nfe2l2; id2 | 6.642 | 3.406-13.468 | 3 | 0 |
| **GO:0071372**cellular response to follicle-stimulating hormone stimulus | 3/19 | 16% | inhba; id2; egr1 | 8.263 | 1.517-45.905 | 1 | 2 |
| **GO:0014910**regulation of smooth muscle cell migration | 3/50 | 6% | nfe2l2; igfbp3; egr1 | 8.263 | 3.406-45.905 | 1 | 2 |
| **GO:0097237**cellular response to toxic substance | 4/80 | 5% | ugt2b1; nqo1; nfe2l2; egr1 | 16.188 | 7.373-41.474 | 3 | 1 |
| **GO:0045598**regulation of fat cell differentiation | 3/42 | 7% | trib3; lpl; id2 | 16.895 | 6.465-58.991 | 2 | 1 |
| **GO:0034976**response to endoplasmic reticulum stress | 3/58 | 5% | trib3; nfe2l2; ccnd1 | 16.895 | 6.465-58.991 | 2 | 1 |
| **GO:0009404**toxin metabolic process | 3/17 | 18% | nfe2l2; cyp1a1; akr7a3 | 19.850 | 12.797-32.354 | 3 | 0 |
| **GO:0098754**detoxification | 5/58 | 9% | nqo1; nfe2l2; gstm2; gsr; akr7a3 | 19.850 | 12.797-32.354 | 5 | 0 |

Official gene symbols from the Rat Genome Database are shown in the “Active Genes” column. Definitions of Gene Ontology terms were provided by the Gene Ontology Resource (http://geneontology.org/).

**GO process description version:** https://cebs.niehs.nih.gov/cebs/study/002-00600-0002-000-0 V04132020

**GO:0030278 regulation of ossification:** Any process that modulates the frequency, rate or extent of ossification, the formation of bone or of a bony substance or the conversion of fibrous tissue or of cartilage into bone or a bony substance.

**GO:0001822 kidney development:** The process whose specific outcome is the progression of the kidney over time, from its formation to the mature structure. The kidney is an organ that filters the blood and/or excretes the end products of body metabolism in the form of urine.

**GO:1903707 negative regulation of hemopoiesis:** Any process that stops, prevents or reduces the frequency, rate or extent of hemopoiesis.

**GO:0071372 cellular response to follicle-stimulating hormone stimulus:** Any process that results in a change in state or activity of a cell (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of a follicle-stimulating hormone stimulus.

**GO:0014910 regulation of smooth muscle cell migration:** Any process that modulates the frequency, rate or extent of smooth muscle cell migration.

**GO:0097237 cellular response to toxic substance:** Any process that results in a change in state or activity of a cell (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of a toxic stimulus.

**GO:0045598 regulation of fat cell differentiation:** Any process that modulates the frequency, rate or extent of adipocyte differentiation.

**GO:0034976 response to endoplasmic reticulum stress:** Any process that results in a change in state or activity of a cell (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of a stress acting at the endoplasmic reticulum. ER stress usually results from the accumulation of unfolded or misfolded proteins in the ER lumen.

**GO:0009404 toxin metabolic process:** The chemical reactions and pathways involving a toxin, a poisonous compound (typically a protein) that is produced by cells or organisms and that can cause disease when introduced into the body or tissues of an organism.

**GO:0098754 detoxification:** Any process that reduces or removes the toxicity of a toxic substance. These may include transport of the toxic substance away from sensitive areas and to compartments or complexes whose purpose is sequestration of the toxic substance.

### Female Liver Top 10 GO Biological Process Gene Sets Ranked by Potency of Perturbation (Sorted by BMD Median)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Category Name** | Input Genes/Platform Genes in Gene Set | % Gene Set Coverage | Active Genes | BMD1std Median of Gene Set Transcripts (mg/kg) | Median BMDL1Std-BMDU1Std (mg/kg) | Genes with Changed Direction Up | Genes with Changed Direction Down |
| **GO:0071103**DNA conformation change | 3/32 | 9% | top2a; mcm6; mcm2 | 1.874 | 0.497-9.530 | 3 | 0 |
| **GO:0051276**chromosome organization | 5/90 | 6% | top2a; mcm6; mcm2; kif22; gar1 | 1.874 | 0.497-9.530 | 5 | 0 |
| **GO:0006281**DNA repair | 4/74 | 5% | mms22l; mcm6; mcm2; kif22 | 2.822 | 0.727-15.213 | 4 | 0 |
| **GO:0000724**double-strand break repair via homologous recombination | 3/15 | 20% | mms22l; mcm6; mcm2 | 3.769 | 0.956-20.896 | 3 | 0 |
| **GO:0006259**DNA metabolic process | 7/119 | 6% | top2a; mms22l; mcm6; mcm2; kif22; gar1; cyp1b1 | 3.769 | 0.956-20.896 | 7 | 0 |
| **GO:0009066**aspartate family amino acid metabolic process | 4/14 | 29% | phgdh; bhmt; asns; aass | 5.933 | 2.674-26.084 | 2 | 2 |
| **GO:0042737**drug catabolic process | 5/60 | 8% | pck2; hba-a1; hba-a2; gpx1; aass | 8.004 | 2.700-37.943 | 1 | 4 |
| **GO:0010639**negative regulation of organelle organization | 5/89 | 6% | top2a; mcm2; insig1; gpx1; gclc | 8.004 | 2.700-25.225 | 4 | 1 |
| **GO:0045833**negative regulation of lipid metabolic process | 3/34 | 9% | insig1; esr1; apoc3 | 12.540 | 3.750-51.297 | 1 | 2 |
| **GO:1901607**alpha-amino acid biosynthetic process | 6/19 | 32% | pycr1; psat1; phgdh; bhmt; asns; aass | 16.607 | 6.379-70.854 | 4 | 2 |

Official gene symbols from the Rat Genome Database are shown in the “Active Genes” column. Definitions of Gene Ontology terms were provided by the Gene Ontology Resource (http://geneontology.org/).

**GO process description version:** https://cebs.niehs.nih.gov/cebs/study/002-00600-0002-000-0 V04132020

**GO:0071103 DNA conformation change:** A cellular process that results in a change in the spatial configuration of a DNA molecule. A conformation change can bend DNA, or alter the, twist, writhe, or linking number of a DNA molecule.

**GO:0051276 chromosome organization:** A process that is carried out at the cellular level that results in the assembly, arrangement of constituent parts, or disassembly of chromosomes, structures composed of a very long molecule of DNA and associated proteins that carries hereditary information. This term covers covalent modifications at the molecular level as well as spatial relationships among the major components of a chromosome.

**GO:0006281 DNA repair:** The process of restoring DNA after damage. Genomes are subject to damage by chemical and physical agents in the environment (e.g. UV and ionizing radiations, chemical mutagens, fungal and bacterial toxins, etc.) and by free radicals or alkylating agents endogenously generated in metabolism. DNA is also damaged because of errors during its replication. A variety of different DNA repair pathways have been reported that include direct reversal, base excision repair, nucleotide excision repair, photoreactivation, bypass, double-strand break repair pathway, and mismatch repair pathway.

**GO:0000724 double-strand break repair via homologous recombination:** The error-free repair of a double-strand break in DNA in which the broken DNA molecule is repaired using homologous sequences. A strand in the broken DNA searches for a homologous region in an intact chromosome to serve as the template for DNA synthesis. The restoration of two intact DNA molecules results in the exchange, reciprocal or nonreciprocal, of genetic material between the intact DNA molecule and the broken DNA molecule.

**GO:0006259 DNA metabolic process:** Any cellular metabolic process involving deoxyribonucleic acid. This is one of the two main types of nucleic acid, consisting of a long, unbranched macromolecule formed from one, or more commonly, two, strands of linked deoxyribonucleotides.

**GO:0009066 aspartate family amino acid metabolic process:** The chemical reactions and pathways involving amino acids of the aspartate family, comprising asparagine, aspartate, lysine, methionine and threonine.

**GO:0042737 drug catabolic process:** The chemical reactions and pathways resulting in the breakdown of a drug, a substance used in the diagnosis, treatment or prevention of a disease.

**GO:0010639 negative regulation of organelle organization:** Any process that decreases the frequency, rate or extent of a process involved in the formation, arrangement of constituent parts, or disassembly of an organelle.

**GO:0045833 negative regulation of lipid metabolic process:** Any process that stops, prevents, or reduces the frequency, rate or extent of the chemical reactions and pathways involving lipids.

**GO:1901607 alpha-amino acid biosynthetic process:** The chemical reactions and pathways resulting in the formation of an alpha-amino acid.